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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/940,632	09/30/97	VALLE	001200-2

HM11/1202
GENENCOR INTERNATIONAL, INC
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EXAMINER
PROUTY, R

ART UNIT	PAPER NUMBER
1602	21

DATE MAILED:

12/02/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.

08/940,692

Applicant(s)

Valle et al.

Examiner

Rebecca Prouty

Group Art Unit

1652



THE PERIOD FOR RESPONSE: [check only a) or b)]

- a) ☐ expires _____ months from the mailing date of the final rejection.
- b) ☐ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

- ☒ Appellant's Brief is due two months from the date of the Notice of Appeal filed on Nov 8, 1999 (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on Oct 13, 1999 has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:

- ☒ The proposed amendment(s):

☐ will be entered upon filing of a Notice of Appeal and an Appeal Brief.

- ☒ will not be entered because:

- ☒ they raise new issues that would require further consideration and/or search. (See note below).
- ☐ they raise the issue of new matter. (See note below).
- ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.
- ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: deletion of the type of mutation made in the host cell from Claim 38 raises new issues of completeness and scope of enablement of the claim as many mutations would not result in a Pts-/glu+ cell.

- ☒ Applicant's response has overcome the following rejection(s):

Rejection of Claim 39 under 35 USC 103.

- ☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.

- ☒ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:
see attached

- ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

- ☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):

Claims allowed: none

Claims objected to: 39

Claims rejected: 23-38

- ☐ The proposed drawing correction filed on _____ ☐ has ☐ has not been approved by the Examiner.

- ☐ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

- ☒ Other Interview Summary

Rebecca Prouty
REBECCA PROUTY
PRIMARY EXAMINER
ART UNIT 1652

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Applicants argue that Claims 23, 27, 28, and 38 are novel as Saier et al. did not select for fast growing cells having a growth rate of at least about 0.4/hr. This is not persuasive because the cells isolated by Saier et al. are fast growing as claimed. Table 1 shows that the PTS⁻/glu⁺ mutants have a generation time of 2 hrs. Applicants argue that a doubling time of 2 hours does not meet the limitation of a specific growth rate of at least about 0.4 hr⁻¹. This is not persuasive because a doubling time of 2 hrs as disclosed by Saier et al. is equivalent to a specific growth rate of 0.35 hr⁻¹. This clearly falls within the scope of at least about 0.4 hr⁻¹.

Applicant's argue that the 103 rejection of Claims 23-38 should be withdrawn as the cited references fail to provide sufficient motivation to increase PEP availability. This is not persuasive because Ingrahm et al. specifically suggest preventing PEP use by the PTS system (while providing another means of glucose transport) as an approach to increasing the carbon flow into the common aromatic pathway. Ingrahm et al. state in column 1:

"Phosphoenol pyruvate (PEP) is a central intermediate in glucose metabolism, residing at a branch point for the biosynthesis of many compounds of commercial importance. For example, an equimolar amount of PEP is combined with erythrose-4-phosphate to provide the carbon skeleton for aromatic products such as tyrosine,

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phenylalanine, tryptophan, and some vitamins among other compounds."

and further go on to state:

"In many bacteria, PEP is also necessary for the transport of glucose into the cell. Glucose is phosphorylated in a concerted process by a multiprotein-membrane-bound complex termed the phosphotransferase system (PTS). In this process, PEP serves as the source of a high energy phosphate which is ultimately attached to glucose to yield glucose-6-phosphate and pyruvate. During glycolysis in these organisms, half the PEP produced is obligately consumed to provide energy for glucose uptake. this reduces by 50% the amount of PEP available as a source of carbon skeletons for biosynthesis, severely impacting the efficiency of conversion into many desired commercial products."

Finally in column 3, Ingrahm et al. state:

"For example, by modifying an enteric bacteria such as *E. coli* to use an alternative pathway for glucose uptake characteristic of *Z. mobilis*, the output of any synthetic product derived from PEP as a precursor could be doubled because glucose transport into cells would not be obligately coupled to PEP."

Therefore, Ingrahm et al. explicitly suggest the uncoupling of glucose transport and PEP utilization as a means of increasing the carbon flow into the common aromatic pathway. While Ingrahm et al. suggest doing this by a different means than that suggested by applicants, Saier et al. clearly teach that other means of providing glucose transport to a PTS⁻ cell are known in the art. As such it would have been obvious to one of ordinary skill in the art that the same objective explicitly stated in

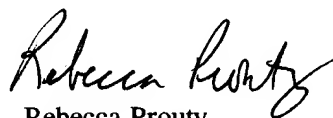
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Ingrahm et al. could be provided by the PTS⁻/glu⁺ cells of Saier et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Rebecca Prouty
Primary Examiner
Art Unit 1652